

REMARKS

The Applicant expresses appreciation for the courtesies extended by Examiner Sean E. Aeder to Applicant's representative Lars Genieser during the telephonic interview on May 25, 2010 (herein, "Interview", summarized in the "Interview Summary" mailed May 28, 2010).

Applicant appreciates the Office Action of April 2, 2010 indicating on pages 2-3 that the spelling of the first inventor's name has been corrected, the objection to the specification has been withdrawn, and the rejections under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 102(b) have been withdrawn.

Applicant respectfully requests reconsideration in light of the amendments above and the remarks that follow.

Claims 1, 5-10, and 16-28 are pending. Claims 6, 8, 10, and 16-19 are withdrawn. Claims 2-4 and 11-15 are canceled. Claims 1, 5, and 28 are amended. Support for amended claims 1, 5, and 28 is found, for example, in paragraphs [0005] and [0037]-[0038] of the specification as filed.

On pages 3-6, the Office Action rejects claims 1, 5, 7, 9, and 20-28 under 35 U.S.C. § 112, first paragraph as allegedly not compliant with the written description requirement. Applicant respectfully traverses for the following reasons.

Applicant submits that the terms "hormone refractory" and "androgen independent" are terms of art, and that in the context of prostate cancer, a person having ordinary skill in the art would understand the two terms to be equivalent. A human or animal suffering from prostate cancer can be subjected to "hormone therapy", a term of art. "Hormone therapy" refers to a course of therapy that lowers the level or reduces the effect of a hormone, for example, an androgen such as testosterone, through the administration of drugs that lower serum testosterone, drugs that act as competitive androgen receptor antagonists, and/or surgical castration. Although initially effective at blocking tumor growth, this hormone therapy eventually fails, in that cancer cells develop that proliferate despite the hormone therapy. This stage of prostate cancer is referred to by those having ordinary skill in the art as "androgen independent" or "hormone refractory" prostate cancer. The terms mean that despite the lowering of testosterone levels or blocking of the effect of testosterone through drugs or surgery, the prostate cancer cells

proliferate despite, that is, independently of or refractory or resistant to, such treatment. The terms originally derive from the context of medical treatment of complex organisms, such as humans or animals, rather than from the context of cellular biology experiments performed under carefully controlled conditions.

The terms "androgen independent" and "hormone refractory" do not have the meaning that cells do not proliferate even when an androgen or hormone is present. That is, a cell is considered to be "hormone refractory" when it continues to proliferate even though a hormone, e.g., testosterone, is reduced to a very low level. If an increased rate of proliferation is observed when the same cell is exposed to a higher level of the hormone, the cell is still considered to be hormone refractory. That is, the cell's behavior at reduced levels of hormone determines whether it is characterized as being "hormone refractory" (the cell's behavior at normal or elevated levels of the hormone does not govern the characterization).

As discussed in paragraph [00042] of the specification as filed, the inventors of the present application determined that there must be some binding of androgen ligand to androgen receptors in hormone refractory prostate cancer cells for cells to proliferate. For this reason, the last sentence of paragraph [00042] states that "the widely used term 'androgen-independent' may be a misleading description of HR prostate cancer." This is a critique of the descriptive value of the term, in that the inventors have found that the cells present in the stage of prostate cancer termed "androgen independent" by those of ordinary skill in the art in fact require a small amount of androgen to proliferate. Nevertheless, the suboptimal descriptive value of the term does not alter the fact that there is a distinct type of prostate cancer cell that does not respond to hormone therapy, is generally lethal, and is termed "androgen independent" by those of ordinary skill in the art.

The Applicant does, however, appreciate that although Applicant may use terms as they are commonly understood by those of ordinary skill in the art, there may be value in selecting a term whose meaning is clearer to laypeople than another term, even though the terms are understood to be equivalent by those of ordinary skill in the art. Therefore, Applicant has amended claim 1 to replace the term "androgen-independent" with "hormone refractory", amended claims 5 and 28 to replace the term "ligand-independent" with "ligand refractory", and amended claim 28 to replace the terms "androgen-independent" and "estrogen-independent" with

"androgen refractory" and "estrogen refractory", respectively. The term "refractory" has the meaning of "not responsive to treatment" (see the attached dictionary definition, "refractory", Webster's II: New Riverside University Dictionary, Houghton Mifflin (1988) p. 988) and thus harks back to the original observations in medical treatment from which the term derives. As such, the meaning of the term "hormone refractory" is clear: a disease state not responsive to hormone therapy in which hormone levels are decreased. Therefore, although a person having ordinary skill in the art would understand the terms "androgen independent" and "hormone refractory" in the context of prostate cancer to be equivalent and refer to a state of a prostate cancer that does not respond to hormone therapy and the cancer cells associated therewith, Applicant, at the Examiner's suggestion, has replaced claim terms using "independent" with terms using "refractory".

Applicant submits that paragraph [00037] of the specification as filed discloses engineered cells that meet the limitations of claims 1 and 5 of the present Application. Paragraph [00037] discloses "introduc[ing] an epitope-tagged wildtype AR [androgen receptor] cDNA by retrovirus infection into HS [hormone sensitive] LNCaP human prostate cancer cells" to make LNCaP-AR cells. This meets the requirement of claim 1 of a "mammalian prostate cancer cell express[ing] an exogenous wild type androgen receptor polynucleotide that encodes an androgen receptor polypeptide" and of claim 5 of a "mammalian cancer cell ... stably express[ing] an exogenous wild type polynucleotide that encodes a nuclear receptor protein or polypeptide" (the androgen receptor being a nuclear receptor protein). Paragraph [00037] continues by stating that "[a] three-fold increase in AR levels in LNCaP-AR cells mimics the expression difference observed." This meets the requirement of claim 1 that "[the] total polypeptide level of said androgen receptor polypeptide ... is at least two-fold higher than the endogenous level of androgen receptor ... polypeptide in a hormone-sensitive prostate cancer cell" and of claim 5 that "said increased level of mRNA in said selected mammalian cancer cell is at least two fold higher than the endogenous level of mRNA in said hormone-sensitive mammalian cancer cell." Paragraph [00037] notes that "LNCaP cells infected with the empty vector failed to grow in steroid-depleted, charcoal-stripped serum unless supplemented with 100 pM of the synthetic androgen, R1881," behavior characteristic of the hormone sensitive cell phenotype. By contrast, paragraph [00037] notes that "LNCaP-AR cells grew in at least 80%

lower concentrations of R1881 [and] were also resistant to bicalutamide," this behavior, continued proliferation at lowered hormone levels, being characteristic of the hormone refractory phenotype, as required by claim 1 ("growth of said mammalian prostate cancer cell [being] hormone refractory") and claim 5 ("growth of said selected mammalian cancer cell [being] nuclear receptor ligand refractory").

Paragraph [00011] presents the use of these cells by "contacting the compound to be tested with [the] mammalian prostate cancer cell ... and then comparing one or more characteristics of the mammalian prostate cancer cell ... with the same one or more characteristics of a control mammalian prostate cancer cell to which the compound has not been administered, wherein a difference in ... the one or more characteristics indicates that the compound has an effect on the mammalian prostate cancer cell." Paragraph [00012] discloses that these characteristics can be physiological characteristics. Paragraph [00016] discloses "treating a hormone refractory prostate cancer in a patient [by] administering to the patient an agent that decreases ... the biological function of the androgen receptor," and one of ordinary skill in the art would understand that such treatment necessarily constitutes contacting hormone refractory prostate cancer cells with the agent or compound. Paragraph [00028] relates that a drug may "inhibit ... tumor growth" of cancer cells, for example, hormone refractory prostate cancer cells. Thus, the written description, for example, paragraphs [00011]-[00012], [00016], [00028], and [00037], presents all limitations of claims 1 and 5. The experiment presented in paragraph [00037] conveys to one of ordinary skill in the art that the Applicant was in possession of the subject matter claimed in claims 1 and 5, a method using a cancer cell expressing an exogenous wild type androgen receptor polynucleotide and exhibiting hormone refractory growth.

Because the subject matter of claims 1 and 5 and the remaining claims, which are dependent therefrom, were presented in the written description of the specification as filed, and that one of ordinary skill in the art would therefore understand that the inventors had possession of the claimed invention at the time the application was filed, claims 1 and 5 as amended and claims 7, 9, and 20-28 dependent therefrom comply with 35 U.S.C. § 112, first paragraph. Applicant therefore respectfully requests that the rejection of claims 1, 5, 7, 9, and 20-28 be withdrawn.

Applicant hereby requests continued examination, and the Commissioner for Patents is authorized to charge the fee of \$405 due for a small entity for a Request for Continued Examination (RCE) to Deposit Account Number 22-0261, under Order Number 58086-232451. If any additional fee or any refund is deemed due, for this filing and any filing made hereafter by this firm for this Application, the Commissioner for Patents is authorized to charge the fee or credit the refund to Deposit Account Number 22-0261, under Order Number 58086-232451.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided. Applicant respectfully requests that a Notice of Allowance of all pending claims not withdrawn, claims 1, 5, 7, 9, and 20-28, be timely issued in this case.

Respectfully submitted,



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